Complete Summary

GUIDELINE TITLE

Docetaxel for the treatment of hormone-refractory metastatic prostate cancer.

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Docetaxel for the treatment of hormone-refractory metastatic prostate cancer. London (UK): National Institute for Health and Clinical Excellence (NICE); 2006 Jun. 35 p. (Technology appraisal guidance; no. 101).

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Hormone-refractory metastatic prostate cancer (mHRPC)

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Treatment

CLINICAL SPECIALTY

Oncology
Urology

INTENDED USERS

Advanced Practice Nurses
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To evaluate the clinical effectiveness and cost-effectiveness of docetaxel (Taxotere®, Sanofi-Aventis) in combination with prednisone/prednisolone for the treatment of metastatic hormone-refractory prostate cancer (mHRPC)

TARGET POPULATION

Men with hormone refractory metastatic prostate cancer

INTERVENTIONS AND PRACTICES CONSIDERED

Docetaxel

MAJOR OUTCOMES CONSIDERED

- Clinical effectiveness
  - Overall survival
  - Progression-free survival
  - Response rate (including complete and partial response)
  - Prostate screening antigen (PSA) decline
  - Adverse effects of treatment
  - Pain
  - Health-related quality of life
- Cost-effectiveness

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases
Searches of Unpublished Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The assessment report for this technology appraisal was prepared by the Centre for Reviews and

Dissemination/Centre for Health Economics (CRD/CHE) Technology Assessment Group, University of York (See the "Availability of Companion Documents" field.)

Search Strategy

A scoping search was conducted which identified a study of docetaxel plus prednisone versus mitoxantrone plus prednisone. The scoping search, however, did not identify any trials comparing docetaxel plus prednisone/prednisolone with any of the other relevant treatments. Trials comparing mitoxantrone (Novantrone®, Wyeth) with other chemotherapies and corticosteroids (used as best supportive care) were identified. Therefore, in order to allow for a comparison between docetaxel and other relevant treatments, the clinical effectiveness and cost-effectiveness of mitoxantrone, the common comparator to these other treatments, was also reviewed.

Sources

Searches were undertaken on the following databases to identify relevant clinical and cost-effectiveness literature. Full details of the search strategies are reported in Appendix 10.1 of the Assessment Report (see "Availability of Companion Documents" field).

- Ovid MEDLINE and Ovid MEDLINE In Process And Other Non-Indexed Citations (Ovid Online – www.ovid.com)
- EMBASE (Ovid Online – www.ovid.com)
- Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library on cd-rom)
- The Cochrane Database of Systematic Reviews (CDSR) (The Cochrane Library on cd-rom)
- National Research Register (NRR) (cd-rom)
- Health Technology Assessment Database (HTA) (Centre for Reviews and Dissemination [CRD] administration database)
- National Health Service Economic Evaluation Database (NHS EED) (CRD administration database)
- Database of Abstracts of Reviews of Effects (DARE) (CRD administration database)
- Cumulative Index to Nursing and Allied Health Literature (CINAHL) (Ovid Online – www.ovid.com)
- Health Management Information Consortium (HMIC) (Ovid Online – www.ovid.com)
- ISI Science and Technology Proceedings (Internet - Web of Knowledge - http://wos.mimas.ac.uk/)
- Social Science Citation Index (Internet - Web of Knowledge - http://wos.mimas.ac.uk/)
- Index to Theses (Internet - http://www.theses.com/)
- SIGLE (SilverPlatter ARC2 – http://www.ovid.com)
- Inside Conferences (DialogLink - http://www.dialog.com/)
- BIOSIS Previews (DialogLink - http://www.dialog.com/)
- Current Controlled Trials (Internet - http://controlled-trials.com/)
- ClinicalTrials.gov (Internet - http://clinicaltrials.gov/)

Searches were also undertaken on several Internet resources.

- International Cancer Research Portfolio (ICRP) (Internet - http://www.cancerportfolio.org/)
- National Cancer Institute Clinical Trials PDQ (Internet http://www.cancer.gov/Search/SearchClinicalTrialsAdvanced.aspx)
- American Society of Clinical Oncology (Internet - http://www.asco.org)

Terminology

The terms for the search strategies were identified through discussion between an information officer and the rest of the research team, by scanning the background literature, and by browsing the MEDLINE thesaurus (Medical Subject Headings [MeSH]). All databases were searched from their inception to the date of the search. Searches took place during April 2005 (see Appendix 10.1 of the Assessment Report [see "Availability of Companion Documents" field] for dates of individual searches). No language or other restrictions were applied.

Management of References

As several databases were searched, some degree of duplication resulted. In order to manage this issue, the titles and abstracts of bibliographic records were downloaded and imported into Endnote bibliographic management software to allow for the removal of duplicate records.

Handsearching

The bibliographies of all included studies, the industry submission and papers retrieved for background information were reviewed to identify further relevant studies.

Results

The literature searches retrieved 1065 references. All references were managed using Endnote software version 6. The full details of the search strategies are given in Appendix 10.1 of the Assessment Report (see "Availability of Companion Documents" field).

Inclusion and Exclusion Criteria

Two reviewers independently screened all titles and abstracts. Full paper manuscripts of any titles/abstracts that were considered relevant by either reviewer were obtained where possible. The relevance of each study was assessed according to the criteria set out below. Studies that did not meet all the criteria were excluded and their bibliographic details listed with reasons for exclusion in Appendix 10.2 of the Assessment Report (see "Availability of Companion Documents" field). Any discrepancies were resolved by consensus and if necessary a third reviewer was consulted.

Interventions

This review covered the effectiveness of the following two alternative chemotherapeutic agents:

- Docetaxel (Taxotere®, Sanofi-Aventis) in combination with prednisone/prednisolone, which is within its licensed indication.
- Mitoxantrone (Novantrone®, Wyeth) in combination with a corticosteroid, which is not licensed for use in this patient group in the United Kingdom (UK). Mitoxantrone is licensed in combination with corticosteroids for metastatic hormone-refractory metastic prostate cancer (mHRPC) in the United States of America (USA). In order to be inclusive, the Assessment Group assessed mitoxantrone in combination with any form of corticosteroid, since it is not licensed for hormone-refractory metastatic prostate cancer in the United Kingdom, its use is not restricted to be in combination with prednisone/prednisolone.

Comparators

The comparators that were considered included any chemotherapy regimen, best supportive care (which may include radiotherapy, corticosteroids, oxygen, antibiotics and analgesics), or placebo.

Participants

Men with metastatic hormone-refractory prostate cancer (mHRPC).

Study Design

Randomised controlled trials that compared docetaxel in combination with prednisone/prednisolone or mitoxantrone in combination with a corticosteroid with any chemotherapy regimen, best supportive care (which may include radiotherapy, corticosteroids, oxygen, antibiotics and analgesics), or placebo.

For the assessment of cost-effectiveness a broader range of studies were considered including economic evaluations conducted alongside trials, modelling studies and analyses of administrative databases. Only full economic evaluations that compared two or more options and considered both costs and consequences (including cost-effectiveness, cost-utility and cost-benefit analysis) were included.

Outcomes

Data on the following outcomes were included:

- Overall survival
- Progression-free survival
- Response rate (including complete and partial response)
- Prostate surface antigen (PSA) decline
- Adverse effects of treatment
- Pain
- Health-related quality of life

Publication

A full English language paper copy or trial report of the study had to be available for it to be included in the review. Studies which were reported in abstract form

only, and where no further information was available, were excluded. Descriptions of these studies are provided in Appendix 10.3 of the Assessment Report (see "Availability of Companion Documents" field). Foreign language papers were also excluded.

NUMBER OF SOURCE DOCUMENTS

Clinical Effectiveness

Seven randomized controlled trials (RCTs) were identified that met inclusion criteria. Three of these trials used docetaxel compared to mitoxantrone plus prednisone, three trials used mitoxantrone plus a corticosteroid compared to a corticosteroid, and one trial used mitoxantrone plus prednisone compared to mitoxantrone plus prednisone plus clodronate.

Cost Effectiveness

The systematic literature search identified only one study which met the criteria for inclusion in the cost-effectiveness review. A separate cost-effectiveness analysis was also submitted by the manufacturers (Sanofi-Aventis).

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis of Randomized Controlled Trials
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The assessment report for this technology appraisal was prepared by the Centre for Reviews and Dissemination/Centre for Health Economics (CRD/CHE) Technology Assessment Group, University of York (See the "Availability of Companion Documents" field.)

Data Extraction and Quality Assessment

Data from included studies were extracted by one reviewer and independently checked for accuracy by a second reviewer. Individual studies were assessed for quality by one reviewer and independently checked for accuracy by a second reviewer.

Methods of Analysis/Synthesis

The results of the data extraction and quality assessment for each study of clinical effectiveness are presented in structured tables and as a narrative summary. Where appropriate, outcomes were synthesised using formal analytic approaches. For the cost-effectiveness section of the report, details of each identified published economic evaluation, together with a critical appraisal of its quality, are presented in structured tables. A new cost-effectiveness model was developed in order to establish the cost-effectiveness of docetaxel compared with a range of potential comparators.

Handling the Company Submissions

No substantive additional clinical effectiveness data were presented in the company submission. The economic evaluation included in the company submission was assessed and used to inform the development of the new model.

For a complete discussion of the methods used to analyse the evidence, see section 3.5 in the Assessment Report (see "Availability of Companion Documents" field).

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Clinical Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and

the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE website. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

Cost Effectiveness

- The manufacturer (Sanofi-Aventis) and the Assessment Group provided estimates of cost effectiveness. Some consultees commented on economic issues. The Assessment Group developed its own economic model and critiqued the model submitted by Sanofi-Aventis.
- The Assessment Group's literature search did not yield any suitable cost-effectiveness studies of docetaxel-based treatment regimens. One study was found that compared mitoxantrone and prednisone with prednisone alone and was based on the CCI-NOV-22 randomized controlled trial (RCT). That study was used to inform the follow-up costs of the Assessment Group's economic model.

See section 4.2 in the original guideline document for a complete summary of the evidence of cost effectiveness from the manufacturer and the economic evaluation undertaken by the Assessment Group.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Consultee organizations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination.

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

- Docetaxel is recommended, within its licensed indications, as a treatment option for men with hormone-refractory metastatic prostate cancer only if their Karnofsky performance-status score is 60% or more.
- It is recommended that treatment with docetaxel should be stopped:
    - At the completion of planned treatment of up to 10 cycles, or
    - If severe adverse events occur, or
    - In the presence of progression of disease as evidenced by clinical or laboratory criteria, or by imaging studies.
- Repeat cycles of treatment with docetaxel are not recommended if the disease recurs after completion of the planned course of chemotherapy.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is not specifically stated.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of docetaxel for the treatment of hormone-refractory metastatic prostate cancer

POTENTIAL HARMS

Reported adverse effects of docetaxel include hypersensitivity reactions (presenting as flushing, skin reactions, hypotension, and bronchospasm), bone marrow suppression (neutropenia, thrombocytopenia, anaemia), cutaneous reactions, fluid retention, peripheral neuropathy, alopecia, cardiac disorders, and tiredness.

For full details of side effects and contraindications, see the Summary of Product Characteristics for each drug, available at http://emc.medicines.org.uk/

CONTRAINDICATIONS

CONTRAINDICATIONS

Contraindications to docetaxel include severe allergic reaction, low white blood cell count due to bone-marrow damage (myelosuppression), or severe liver disease. Premedication with a corticosteroid is usually recommended to help prevent allergic reaction.

For full details of side effects and contraindications, see the Summary of Product Characteristics for each drug, available at http://emc.medicines.org.uk/

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This guidance represents the view of the Institute, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. The guidance does not, however, override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation and Audit

- National Health Service (NHS) organisations and clinicians who care for men with prostate cancer should review their current practice and policies to take account of the guidance (see the "Major Recommendations" field).
- Local guidelines, protocols, or care pathways that refer to the care of men with prostate cancer should incorporate the guidance.

- To measure compliance locally with the guidance, the following criteria could be used. Further details on suggestions for audit are presented in appendix C of the original guideline document.
    - A man with hormone-refractory metastatic prostate cancer is offered docetaxel, within its licensed indications, as a treatment option only if his Karnofsky performance-status score is 60% or more.
    - For a man with hormone-refractory metastatic prostate cancer who is treated with docetaxel, treatment with docetaxel is stopped when any of the following circumstances occur:
        - Planned treatment of up to 10 cycles is completed, or
        - The man experiences a severe adverse event, or
        - There is evidence of progression of disease
    - Repeat cycles of treatment with docetaxel are not provided if the disease recurs after completion of the planned course of chemotherapy

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Patient Resources
Quick Reference Guides/Physician Guides
Resources

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Docetaxel for the treatment of hormone-refractory metastatic prostate cancer. London (UK): National Institute for Health and Clinical Excellence (NICE); 2006 Jun. 35 p. (Technology appraisal guidance; no. 101).

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2006 Jun

GUIDELINE DEVELOPER(S)

National Institute for Health and Clinical Excellence (NICE) - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

National Institute for Health and Clinical Excellence (NICE)

GUIDELINE COMMITTEE

Appraisal Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Committee Members: Dr Jane Adam, Radiologist, St George's Hospital, London; Professor A E Ades, MRC Senior Scientist, MRC Health Services Research Collaboration, Department of Social Medicine, University of Bristol; Dr Tom Aslan, General Practitioner, Stockwell, London; Professor David Barnett (*Chair*) Professor of Clinical Pharmacology, University of Leicester; Mrs Elizabeth Brain, Lay Representative; Dr Karl Claxton, Health Economist, University of York; Dr Richard Cookson, Senior Lecturer in Health Economics, School of Medicine Health Policy and Practice, University of East Anglia; Mrs Fiona Duncan, Clinical Nurse Specialist, Anaesthetic Department, Blackpool Victoria Hospital; Professor Christopher Eccleston, Director, Pain Management Unit, University of Bath; Dr Paul Ewings, Statistician, Taunton & Somerset NHS Trust, Taunton; Professor Terry Feest, Professor of Clinical Nephrology, Southmead Hospital, Bristol; Professor John Geddes, Professor of Epidemiological Psychiatry, University of Oxford; Mr John Goulston, Director of Finance, Barts and the London NHS Trust; Mr Adrian Griffin, Health Outcomes Manager, Johnson & Johnson Medical; Ms Linda Hands, Consultant Surgeon, John Radcliffe Hospital, Oxford; Dr Elizabeth Haxby, Lead Clinician in Clinical Risk Management, Royal Brompton Hospital, London; Dr Rowan Hillson, Consultant Physician, Diabeticare, The Hillingdon Hospital, Uxbridge; Dr Catherine Jackson, Clinical Senior Lecturer in Primary Care Medicine, Alyth Health Centre, Angus, Scotland; Professor Richard Lilford, Professor of Clinical Epidemiology, Department of Public Health and Epidemiology, University of Birmingham; Dr Simon Mitchell, Consultant Neonatal Paediatrician, St Mary's Hospital, Manchester; Ms Judith Paget, Chief Executive, Caerphilly Local Health Board, Wales; Dr Katherine Payne, Health Economist, The North West Genetics Knowledge Park, The University of Manchester; Dr Ann Richardson, Lay Representative; Professor Philip Routledge, Professor of Clinical Pharmacology, College of Medicine, University of Wales, Cardiff; Dr Stephen Saltissi, Consultant Cardiologist, Royal Liverpool University Hospital; Mr Mike Spencer, General Manager, Clinical Support Services, Cardiff and Vale NHS Trust; Dr Debbie Stephenson, Head of HTA Strategy, Eli Lilly and Company; Professor Andrew Stevens (*Vice Chair*) Professor of Public Health, University of Birmingham; Dr Cathryn Thomas, General Practitioner, and Associate Professor, Department of

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) format from the National Institute for Health and Clinical Excellence (NICE) Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Docetaxel for the treatment of hormone refractory metastatic prostate cancer. Quick reference guide. London (UK): National Institute for Health and Clinical Excellence (NICE); 2006 Jun. 2 p. (Technology appraisal 101). Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.
- Costing template and costing report. Docetaxel for the treatment of hormone-refractory metastatic prostate cancer. London (UK): National Institute for Health and Clinical Excellence (NICE); 2006 Jun. Various p. (Technology appraisal 101). Available in Portable Document Format (PDF) from the NICE Web site.
- A systematic review and economic model of the effectiveness and cost-effectiveness of docetaxel in combination with prednisone or prednisolone for the treatment of hormone-refractory metastatic prostate cancer. Assessment report. Centre for Reviews and Dissemination/Centre for Health Economics (CRD/CHE) Technology Assessment Group, University of York. 2005 Sep. Electronic copies: Available from the NICE Web site.

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N1056. 11 Strand, London, WC2N 5HR.

PATIENT RESOURCES

The following is available:

- Docetaxel for the treatment of hormone-refractory metastatic prostate cancer. Understanding NICE guidance. Information for people who use NHS services. London (UK): National Institute for Health and Clinical Excellence (NICE); 2006 Jun. 4 p. (Technology appraisal 101).

Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.

Print copies: Available from the NHS Response Line 0870 1555 455. ref: N1057. 11 Strand, London, WC2N 5HR.

NGC STATUS

This NGC summary was completed by ECRI on March 12, 2007.

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Date Modified: 10/6/2008